

CLAIMS

1. A polypeptide having the ability to bind CEA comprising a CEA binding loop having the amino acid sequence Cys-X₄-X₅-X₆-X₇-X₈-X₉-X₁₀-X₁₁-Cys (SEQ ID NO: 3),

wherein

X₄ is Asn, Glu, or Met;
X₅ is Asn, Leu, Met or Phe;
X₆ is Asp, Gly, Ile, Lys Phe or Thr;
X₇ is Ala, Gln, Gly, Lys or Thr;
X₈ is Arg, Asn, Asp, Glu or Gly;
X₉ is Gln, Gly or Leu;
X₁₀ is Ala, Trp or Tyr;
X₁₁ is Ala, Gly, His, Phe, Thr or Val;

2. A polypeptide according to Claim 1, wherein

X₄ is Glu;
X₅ is Asn, Leu, Met or Phe;
X₆ is Asp, Gly, Ile, Lys, Phe or Thr;
X₇ is Lys;
X₈ is Arg, Asn, Asp, Glu or Gly;
X₉ is Gln;
X₁₀ is Trp; and
X₁₁ is Ala, Gly, His, Phe, Thr or Val.

3. A polypeptide according to Claim 1, comprising the amino acid sequence:

X₁ X₂ X₃-Cys X₄ X₅-X₆-X₇-X₈-X₉-X₁₀-X₁₁-Cys-X₁₂-X₁₃-X₁₄ (SEQ ID NO:1),

wherein

X_1 is Asn or Asp;
 X_2 is Trp;
 X_3 is Asp, Phe or Val;
 X_4 is Asn, Glu or Met;
 X_5 is Asn, Leu, Met or Phe;
 X_6 is Asp, Gly, Ile, Lys, Phe or Thr;
 X_7 is Ala, Gln, Gly, Lys or Thr;
 X_8 is Arg, Asn, Asp, Glu or Gly;
 X_9 is Gln, Gly or Leu;
 X_{10} is Ala, Trp or Tyr;
 X_{11} is Ala, Gly, His, Phe, Thr or Val;
 X_{12} is Asn, Gln, Phe, Ser or Val;
 X_{13} is Arg, Leu, Pro or Ser; and
 X_{14} is Leu, Ser, Trp or Tyr.

4. A polypeptide according to Claim 3, having the amino acid sequence:

X_1 -Trp-Val-Cys-Glu- X_5 - X_6 -Lys- X_8 -Gln-Trp- X_{11} -Cys-Asn- X_{13} - X_{14} (SEQ ID NO:2), wherein

X_1 is Asn or Asp;
 X_5 is Asn, Leu, Met or Phe;
 X_6 is Asp, Gly, Ile, Lys, Phe or Thr;
 X_8 is Arg, Asn, Asp, Glu or Gly;
 X_{11} is Ala, Gly, His, Phe, Thr or Val;
 X_{13} is Arg, Leu, Pro or Ser; and
 X_{14} is Leu or Tyr.

5. A polypeptide according to Claim 3, comprising an amino acid sequence selected from the group consisting of:

Asn-Trp-Val-Cys-Asn-Leu-Phe-Lys-Asn-Gln-Trp-Phe Cys Asn-Ser-Tyr
 (SEQ ID NO:4),

Asp-Trp-Val-Cys-Glu-Asn-Lys-Lys-Asp-Gln-Trp-Thr-Cys-Asn-Leu-Leu
(SEQ ID NO:5),

Asn-Trp-Asp-Cys-Met-Phe-Gly-Ala-Glu-Gly-Trp-Ala-Cys-Ser-Pro-Trp
(SEQ ID NO:6);

Asp-Trp-Val-Cys-Glu-Lys-Thr-Thr-Gly-Gly-Tyr-Val-Cys-Gln-Pro-Lcu
(SEQ ID NO:7);

Asn-Trp-Phe-Cys-Glu-Met-Ile-Gly-Arg-Gln-Trp-Gly-Cys-Val-Pro-Ser
(SEQ ID NO:8); and

Asp-Trp-Val-Cys-Asn-Phe-Asp-Gln-Gly-Leu-Ala-His-Cys-Phe-Pro-Ser
(SEQ ID NO:9).

6. A polypeptide having the ability to bind CEA comprising the amino acid
sequence: $X_1-X_2-X_3-Cys-X_4-X_5-X_6-X_7-X_8-X_9-X_{10}-X_{11}-Cys-X_{12}-X_{13}-X_{14}$
(SEQ ID NO:1),

wherein

X_1 is Asp, Asn, Ala, or Ile;

X_2 is Trp;

X_3 is Val, Ile, Met, Tyr, Phe, Pro, or Asp;

X_4 is Asn, Glu, or Asp;

X_5 is Leu, Phe, Tyr, Trp, Val, Met, Ile, or Asn;

X_6 is Phe, Leu, Asp, Glu, Ala, Ile, Lys, Asn, Ser, Val, Trp, or Tyr;

X_7 is Lys, Phe, Asp, Gly, Leu, Asn, or Trp;

X_8 is Asn, Pro, Phe, Gly, Asp, Ala, Ser, Glu, Gln, or Trp;

X_9 is Gln, or Lys;

X_{10} is Trp;

X_{11} is Phe, Thr, Met, Ser, Ala, Asn, Val, His, Ile, Pro, Trp, or Tyr;

X_{12} is Asn, Asp, Glu, Pro, Gln, or Ser;

X_{13} is Val, Leu, Ile, Pro, Ala, Gln, Ser, Met, Glu, Thr, Lys, or Trp; and

X_{14} is Leu, Met, Val, Tyr, Ala, Ile, Trp, His, Pro, Gln, Glu, Phe, Lys, or
Arg.

7. A polypeptide according to Claim 6, comprising an amino acid sequence as depicted in Table 5 (SEQ ID NOs:37-107).
8. A polypeptide according to Claim 1, 3 or 6, wherein said polypeptide binds to CEA but does not bind to NCA.
9. A polypeptide according to Claim 1, 3 or 6, wherein said polypeptide has a K_d for CEA which less than 7 μ M.
10. A method of detecting CEA in a subject comprising the steps of:
 - a) detectably labeling a polypeptide according to any one of Claims 1-7;
 - b) administering to said subject the labeled polypeptide; and, thereafter,
 - c) detecting the labeled polypeptide in the subject.
11. The method according to Claim 10, wherein said polypeptide is labeled with a radioactive compound.
12. The method according to Claim 11, wherein said radioactive compound includes indium.
13. The method according to Claim 11, wherein said radioactive compound includes technetium.
14. The method according to Claim 10, wherein said detecting step is indicative of colon cancer, breast cancer, lung cancer, cervical cancer, ovarian cancer, stomach cancer, bladder cancer, pancreatic cancer or esophageal cancer.

15. A method of treating a CEA associated disease comprising the step of:
administering to a subject in need of treatment for such a disease a composition
comprising a polypeptide according to any one of Claims 1-7 conjugated with a
therapeutic agent effective for treating said disease.
16. The method according to Claim 15, wherein said CEA associated disease is colon
cancer, breast cancer, lung cancer, cervical cancer, ovarian cancer, stomach
cancer, bladder cancer, pancreatic cancer or esophageal cancer.
17. The method according to Claim 15, wherein said therapeutic agent is a radioactive
agent.
18. The method according to Claim 15, wherein said therapeutic agent is a
chemotherapeutic agent.
19. The method according to Claim 15, wherein said therapeutic agent is a toxin or
enzyme.
20. A recombinant bacteriophage expressing exogenous DNA encoding a CEA
binding polypeptide having an amino acid sequence comprising:
 $X_1-X_2-X_3-Cys-X_4-X_5-X_6-X_7-X_8-X_9-X_{10}-X_{11}-Cys-X_{12}-X_{13}-X_{14}$ (SEQ ID
NO:1),
wherein
- X_1 is Asp, Asn, Ala, or Ile;
 - X_2 is Trp;
 - X_3 is Val, Ile, Met, Tyr, Phe, Pro, or Asp;
 - X_4 is Asn, Glu, or Asp;
 - X_5 is Leu, Phe, Tyr, Trp, Val, Met, Ile, or Asn;
 - X_6 is Phe, Leu, Asp, Glu, Ala, Ile, Lys, Asn, Ser, Val, Trp, or Tyr;
 - X_7 is Lys, Phe, Asp, Gly, Leu, Asn, or Trp;

X₈ is Asn, Pro, Phe, Gly, Asp, Ala, Ser, Glu, Gln, or Trp;

X₉ is Gln, or Lys;

X₁₀ is Trp;

X₁₁ is Phe, Thr, Met, Ser, Ala, Asn, Val, His, Ile, Pro, Trp, or Tyr;

X₁₂ is Asn, Asp, Glu, Pro, Gln, or Ser;

X₁₃ is Val, Leu, Ile, Pro, Ala, Gln, Ser, Met, Glu, Thr, Lys, or Trp; and

X₁₄ is Leu, Met, Val, Tyr, Ala, Ile, Trp, His, Pro, Gln, Glu, Phe, Lys, or
Arg

and wherein said binding polypeptide is displayed on the surface of said
bacteriophage.

21. A recombinant bacteriophage according to Claim 20, expressing exogenous DNA
encoding an amino acid sequence selected from the group consisting of:

Asn-Trp-Val-Cys-Asn-Leu-Phe-Lys-Asn-Gln-Trp-Phe-Cys-Asn-
Ser-Tyr (SEQ ID NO:4), and

Asp-Trp-Val-Cys-Glu-Asn-Lys-Lys-Asp-Gln-Trp-Thr-Cys-Asn-
Leu-Leu (SEQ ID NO:5).

22. A recombinant bacteriophage according to Claim 20, expressing exogenous DNA
encoding an amino acid sequence selected from the group of sequences depicted
in Table 5 (SEQ ID NOs: 37-107).